synthesis of the protein product. Earlier this year, Thomas Tuschl and his Max Planck coworkers discovered that an RNAi intermediate, called siRNA (small interfering RNA), instigates degradation of an mRNA in the fruit fly. Tuschl wondered whether that intermediate, a 21-base dsRNA with two bases overhanging on each end, would be better than longer dsRNAs at silencing genes in cultured mammalian cells.

In the new work, Tuschl and his team tested synthetic siRNAs that matched the sequence of four different genes that express cytoskeletal proteins. In four different cell lines derived from human and monkey, expression of three of the four genes was lowered substantially—by as much as 90%. The fourth gene is highly expressed, which may make silencing it more difficult, say the authors. Control genes not targeted by the siRNAs were not affected. The team has subsequently tried RNAi on other genes, and according to co-author Klaus Weber, nine out of 10 genes can be "knocked down" with the method.

This targeted silencing in mammalian cells appears to work by circumventing a global cellular process not present in lower organisms. Injection of long dsRNAs into mammalian cells (which probably mimics invasion by a virus) induces a broad interferon response that reduces the translation of many genes and can even trigger cell suicide. siRNAs appear to be short enough to sneak under the radar of the interferon system but long enough to specifically target single genes.

Still, Zamore cautions that although the technique is promising, it is too soon to know whether it will deliver. Genes are not always turned completely off, for instance, and RNAi may not be effective for genes whose protein products are unusually stable or highly abundant. Fifteen years ago, antisense methods for gene silencing and gene therapy offered similar hopes, but that has largely been a bust. Unlike antisense, however, RNAi seems to take advantage of an existing biological pathway, which just might give it a leg up.

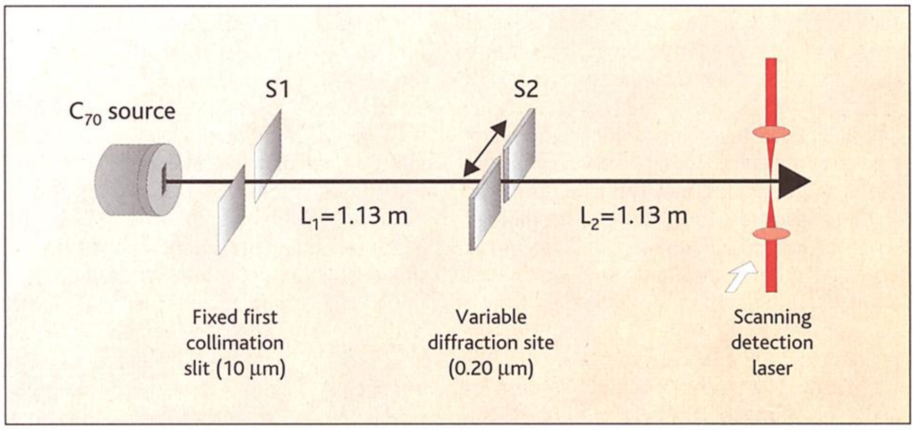
–R. JOHN DAVENPORT

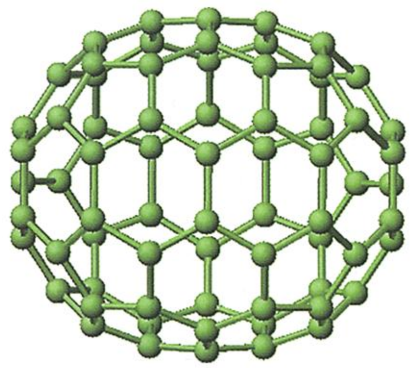
QUANTUM PHYSICS

Microscale Weirdness Expands Its Turf

Schrödinger's pipe dreams aside, no sane physicist would try to do a quantum-mechanical experiment with a cat. A cat is a large object, which tends to follow the classical laws of prequantum physics; quantum mechanics tends to hold sway over small objects, such as atoms. But physicists in Austria are breaking down the tidy distinction between large objects and small ones. In a paper that has been posted on the Los Alamos preprint archives (arXiv.org/abs/quant-ph/0105061) and submitted to *Physical Review Letters*, they show that a cluster of 70 carbon atoms—a veritable monster by quantum-theory standards—is governed by the archquantum law known as the Heisenberg Uncertainty Principle. These clusters are the largest, hottest, and most complicated objects that have been shown to obey Heisenberg's law, and they are helping scientists understand the increasingly fuzzy divide between the quantum and the classical.

Zeilinger and his colleagues decided to probe the hazy border between quantum mechanical and classical by looking at an object that lies between both worlds: the C_{70} molecule. The ungainly bigger brother of C_{60} (buckminsterfullerene), C_{70} is much more massive than the particles that physicists usually use to test the laws of quantum mechanics. At the same time, C_{70} is much smaller than a cat, so it can be stuffed through a small slit with a lot less difficulty. "You don't usually think of looking at such a complex system as quantum," says Monroe, who calls the massive molecule "a nice middle ground."





Rim shot. In a large-scale test of the Uncertainty Principle, narrowing a beam of C_{70} molecules *(right)* made their momenta more varied—just as Werner Heisenberg predicted.

"It's a very good idea to try to cross that boundary," says Christopher Monroe, a physicist at the University of Michigan, Ann Arbor. "I think these are wonderful experiments."

Decades ago, experimenters showed that very small things such as neutrons and protons obey Werner Heisenberg's dictum that the better you understand an object's position, the less you are able to predict its momentum. For example, when you increasingly constrict a beam of neutrons by forcing it through smaller and smaller slits, the particles take on a greater and greater range of possible momenta. As objects get larger, though, the Heisenberg Uncertainty Principle and other quantum effects such as interference become harder to measure. Some physicists, including Roger Penrose of the University of Cambridge, U.K., argue that quantum effects break down as objects get larger, causing big objects to behave classically while small ones behave quantum mechanically. Anton Zeilinger of the University of Vienna in Austria disagrees. "A transition from quantum to classical as you go from micro- to macroscopic … is not going to happen in my expectation," says Zeilinger. "It's just a question of the skill of the experimenter and how much money [there is] to perform the experiment."

Zeilinger's team shot a beam of C_{70} through an adjustable slit whose size ranged from 20 micrometers to 70 nanometers. Using a sensitive laser detector, the researchers measured the range of momenta of the C_{70} molecules that had passed through the slit. When the slit got smaller than 4 micrometers, the C_{70} began to behave like quantum objects: As the slit size decreased, the range of the molecules' momenta got broader and broader. In other words, the more that was known about the molecules' positions, the less was known about their momenta. Despite its size, the C_{70} was behaving "very, very precisely" as a quantum-mechanical object should, says Zeilinger. And although he notes that C_{70} is still too small to disprove Penrose's breakdown theory, it has extended the quantum domain farther than before. "We can work upwards slowly," he says. Cat lovers beware.

–CHARLES SEIFE

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